

Nosocomial Bloodstream Infections in Brazilian Hospitals: Analysis of 2,563 Cases from a Prospective Nationwide Surveillance Study[▽]

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Received 21 February 2011/Returned for modification 28 February 2011/Accepted 3 March 2011

Nosocomial bloodstream infections (nBSIs) are an important cause of morbidity and mortality. Data from a nationwide, concurrent surveillance study, Brazilian SCOPE (Surveillance and Control of Pathogens of Epidemiological Importance), were used to examine the epidemiology and microbiology of nBSIs at 16 Brazilian hospitals. In our study 2,563 patients with nBSIs were included from 12 June 2007 to 31 March 2010. Ninety-five percent of BSIs were monomicrobial. Gram-negative organisms caused 58.5% of these BSIs, Gram-positive organisms caused 35.4%, and fungi caused 6.1%. The most common pathogens (monomicrobial) were *Staphylococcus aureus* (14.0%), coagulase-negative staphylococci (CoNS) (12.6%), *Klebsiella* spp. (12.0%), and *Acinetobacter* spp. (11.4%). The crude mortality was 40.0%. Forty-nine percent of nBSIs occurred in the intensive-care unit (ICU). The most frequent underlying conditions were malignancy, in 622 patients (24.3%). Among the potential factors predisposing patients to BSI, central venous catheters were the most frequent (70.3%). Methicillin resistance was detected in 157 *S. aureus* isolates (43.7%). Of the *Klebsiella* sp. isolates, 54.9% were resistant to third-generation cephalosporins. Of the *Acinetobacter* spp. and *Pseudomonas aeruginosa* isolates, 55.9% and 36.8%, respectively, were resistant to imipenem. In our multicenter study, we found high crude mortality and a high proportion of nBSIs due to antibiotic-resistant organisms.

Nosocomial bloodstream infections (nBSIs) are an important cause of morbidity and mortality (29). The incidences of bloodstream infections (BSIs) are varied (1 to 36%) in different studies (8, 28). The crude mortality is high, particularly for intensive-care unit (ICU) patients (23).

Current guidelines recommend broad-spectrum combination therapy with more than two antibiotics as the initial empirical therapy for some types of infections in patients at risk of being infected with resistant organisms (1). All antibiotics can potentially exert selective pressure and thereby drive resistance, yet appropriate empirical antimicrobial therapy is important, since it can decrease mortality in critically ill patients (12, 14).

The rates of antimicrobial resistance among pathogens causing health care-associated infections are increasing, principally among Gram-negative organisms (*Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and *Klebsiella pneumoniae*) (3). In-

deed this increase in antimicrobial resistance demonstrates a need for surveillance programs to define the species distribution and the resistance patterns of pathogens causing nBSIs, ultimately helping clinicians to choose the most appropriate antimicrobial therapy for hospitalized patients (29).

There are differences in surveillance programs in different parts of the world with regard to methodologies and populations studied (e.g., ICU patients, neutropenic patients, and hemodialysis patients) (13, 27, 29). The purpose of this study was to evaluate the epidemiological features of nBSIs in Brazil and the species distribution and antimicrobial susceptibility of the pathogens, using the same methodology as the U.S. Surveillance and Control of Pathogens of Epidemiologic Importance (SCOPE) program (29).

MATERIALS AND METHODS

Study design. The Brazilian SCOPE (BrSCOPE) is based at Universidade Federal de São Paulo, São Paulo, Brazil, and includes 16 hospitals of various sizes that are geographically dispersed throughout the five different regions of Brazil (north, northeast, middle-east, southeast, and south). Clinical data were concurrently collected by local infection control practitioners using a standardized case report form and forwarded to the coordinating center, along with each

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[▽] Published ahead of print on 16 March 2011.

microbiological isolate. The study period reported on here is 12 June 2007 to 31 March 2010.

A nosocomial BSI was diagnosed if 1 or more cultures of blood sampled at least 48 h after admission yielded a pathogenic organism. If the bloodstream isolate was a potential skin contaminant (e.g., diphtheroids, *Propionibacterium* spp., *Bacillus* spp., coagulase-negative staphylococci, or micrococci), the presence of an intravascular catheter and the initiation of targeted antimicrobial therapy were required for the diagnosis, as well as at least 1 of the following findings: temperature of $>38.0^{\circ}\text{C}$ or $<36^{\circ}\text{C}$, chills, and/or systolic blood pressure of <90 mm Hg. BSI episodes that represented relapses were excluded. We studied the data from all eligible episodes of BSI.

The data that were routinely collected included the patient's age, sex, location at the onset of BSI (ICU versus non-ICU ward), clinical service at the onset of BSI, and predisposing clinical conditions, as well as the identifications and antimicrobial susceptibilities of the causative pathogens and status at discharge. Predisposing clinical conditions that were routinely recorded included neutropenia (defined as an absolute neutrophil count of $<1,000/\mu\text{l}$), peritoneal dialysis or hemodialysis, and presence of intravascular catheters (i.e., central lines, arterial catheters, or peripheral intravenous catheters). Secondary BSIs were regarded as those with a clear source of bacteremia other than a central line. Sources of secondary BSI were identified by cultures of samples (urine, tracheal secretions, intra-abdominal samples, etc.) obtained from distant sites that yielded the same pathogen with an identical resistance pattern. Distant sites were sites where an infection was diagnosed other than a central line (pneumonia, urinary tract infection, abdominal infection, etc.).

Microbiological methods. Blood cultures were processed at the participating hospitals. The identification of blood isolates and susceptibility testing were done by the routine methods in use at the affiliated laboratories. All affiliated laboratories were Brazilian Society of Clinical Pathologists certified, and all microbiological methods used were consistent with current CLSI recommendations (7). Data from all hospitals were used for analysis, and denominators for individual antimicrobial agents may vary, because not all hospitals test and report all drugs. At the reference laboratory, the Special Microbiology Laboratory of Universidade Federal de São Paulo, samples identified by manual methods were subjected to reidentification and antimicrobial susceptibility testing by a Phoenix BD automated system. MIC determination by Etest for oxacillin and carbapenems and agar dilution for vancomycin were done to confirm resistant phenotypes.

Molecular tests were applied to selected resistant strains of methicillin-resistant *Staphylococcus aureus* (MRSA) (*mecA* gene; staphylococcal cassette chromosome *mec* [SCC*mec*] characterization was according to the method of Zhang et al. [30] and Milheirito et al. [19], and molecular typing was done by pulsed field gel electrophoresis [PFGE]), *Enterococcus* spp. (*vanA* and *vanB* genes) (10), *K. pneumoniae* (*bla*_{TEM}, *bla*_{CTX}, and *bla*_{SHV} [6] and *bla*_{KPC} [20] genes), *Acinetobacter* spp. (*bla*_{OXA23} and *bla*_{OXA51} genes) (25), and *P. aeruginosa* (*bla*_{IMP}, *bla*_{VIM}, and *bla*_{SPM} genes) (18).

Statistical analysis. The results were expressed as the mean \pm standard deviation (SD) or as a proportion of the total number of patients or isolates. For continuous variables, mean values were compared, using two sample *t* tests for independent samples. Differences in proportions were compared using a chi-square test or Fisher's exact test, as appropriate. All tests of significance were 2 tailed; α was set at 0.05. All statistical analyses were done using SPSS software (SPSS).

RESULTS

Study population and patient characteristics. During the 2.8-year study period, a total of 2,563 infections with 2,688 organisms were reported by the 16 participating hospitals. Of these, 342 clinically significant episodes of BSI (13.3%) were identified in pediatric patients (≤ 16 years of age). The patients had a mean age of 50.6 ± 24.8 years (range, 0 to 97 years). Fifty-six percent of the patients were male (Table 1).

Approximately one-half (49%) of hospital-acquired BSIs occurred in the ICU. The most frequent underlying conditions (recorded as diagnoses at admission) were malignancy, in 622 patients (24.3%); neurologic conditions, in 309 patients (12.1%); cardiovascular conditions, in 292 patients (11.4%); gastroenterology conditions, in 251 patients (9.8%); respira-

TABLE 1. Characteristics of the 2,563 patients with nBSIs among 16 Brazilian hospitals

Parameter	No. (%)
Patient demographics	
Age (yr; mean \pm SD).....	50.6 \pm 24.8
Male.....	1,438 (56.1)
ICU setting.....	1,257 (49.0)
Monomicrobial infection.....	2,447 (95.5)
Organisms (<i>n</i> = 2,447)	
Gram-negative.....	1,432 (58.5)
Gram-positive.....	867 (35.4)
Fungi.....	148 (6.1)
Underlying conditions	
Malignancy.....	622 (24.3)
Neurologic.....	309 (12.1)
Cardiovascular.....	292 (11.4)
Gastroenterology.....	251 (9.8)
Respiratory.....	230 (9.0)
Renal.....	220 (8.6)
Potential risk factors	
Central venous catheter.....	1,803 (70.3)
Urinary catheter.....	1,051 (41.0)
Ventilator.....	866 (33.8)
Crude mortality.....	1,024 (40.0)

tory conditions, in 230 patients (9.0%); and renal conditions, in 220 patients (8.6%), as shown in Table 1.

Among the potential factors predisposing patients to BSI, intravascular devices were the most frequent. Central venous catheters were present in 1,803 (70.3%) patients, peripheral intravenous catheters were in place in 701 patients (27.4%), and arterial catheters were in place in 52 patients (2.0%). Urinary catheters were present in 1,051 patients (41.0%). A total of 143 patients (5.6%) were receiving parenteral nutrition, and 256 patients (10.0%) required dialysis at the onset of BSI. Most of these patients underwent hemodialysis (228 patients versus 28 who underwent peritoneal dialysis). Mechanical ventilation was necessary for 866 patients (33.8%). Overall, 1,024 patients died during hospitalization, accounting for a crude mortality rate of 40.0% (Table 1).

Microbiological features. Five percent of all episodes of BSI (*n* = 116) were polymicrobial. Of 2,447 monomicrobial episodes, a total of 1,432 (58.5%) were caused by Gram-negative organisms, 867 (35.4%) by Gram-positive organisms, and 148 (6.1%) by fungi, of which 137 (92.6%) were *Candida* spp. (Table 1).

The rank order of the five major pathogens (Table 2) shows that *S. aureus* was the principal organism responsible for nBSIs (15.4%), followed in rank by coagulase-negative staphylococci (CoNS) (13.4%), *Klebsiella* spp. (13.2%), *Acinetobacter* spp. (12.5%), and *P. aeruginosa* (8.9%). CoNS, *Acinetobacter* spp., and *Candida* spp. were more likely to be isolated from patients in ICUs ($P < 0.001$), as were enterococci ($P < 0.05$), whereas *S. aureus* and *Klebsiella* spp. were more common in patients in wards ($P < 0.001$ and $P < 0.05$, respectively). No significant differences were seen for *P. aeruginosa*, *Enterobacter* spp., *Serratia* spp., and *Proteus* spp. (Table 2).

When stratified by clinical service (Table 3), the following patterns emerged: *Klebsiella* spp. and *S. aureus* were the most

TABLE 2. Distribution of pathogens most commonly isolated from monomicrobial nBSIs and associated crude mortality rates for all patients in ICUs and patients in non-ICU wards

Pathogen	% BSI (rank)			Crude mortality (%)		
	Total (n = 2,447)	ICU (n = 1,196)	Non-ICU (n = 1,251)	Total (n = 971)	ICU (n = 656)	Non-ICU (n = 315)
<i>S. aureus</i>	15.4 (1)	12.8 (3) ^a	17.9 (1)	31.0	48.2	24.0
CoNS	13.8 (2)	16.6 (1) ^a	11.2 (3)	32.0	46.5	23.2
<i>Klebsiella</i> spp.	13.2 (3)	11.8 (4) ^b	14.5 (2)	34.7	55.2	24.8
<i>Acinetobacter</i> spp.	12.5 (4)	15.2 (2) ^a	10.0 (4)	52.1	65.5	39.6
<i>P. aeruginosa</i>	8.9 (5)	10.0 (5)	7.9 (5)	48.9	61.5	39.0
<i>Enterobacter</i> spp.	6.1 (6)	5.8 (7)	6.4 (6)	30.2	61.4	17.1
<i>Candida</i> spp.	5.6 (7)	7.4 (6) ^a	3.9 (7)	68.6	85.9	53.4
<i>Enterococcus</i> spp.	4.5 (8)	5.5 (8) ^b	3.6 (9)	49.5	64.2	36.2
<i>Serratia</i> spp.	3.5 (9)	3.2 (9)	3.8 (8)	40.0	60.0	29.1
<i>Proteus</i> spp.	1.6 (10)	1.8 (10)	1.6 (10)	44.7	61.1	30.0

^a *P* < 0.001 for patients in ICU vs. patients in non-ICU wards.^b *P* < 0.05 for patients in ICU vs. patients in non-ICU wards.

TABLE 3. Distribution of nBSIs and most frequently isolated pathogens causing BSIs, by clinical service

Clinical service, class of BSI, and pathogen ^a	No. (%) of BSIs
Internal medicine	
All BSIs.....	507 (19.8) ^b
Monomicrobial BSIs	
<i>S. aureus</i>	134 (26.4)
CoNS.....	86 (17.0)
<i>Klebsiella</i> spp.	67 (13.2)
Adult hematology/oncology	
All BSIs.....	141 (5.5) ^b
Monomicrobial BSIs	
<i>Klebsiella</i> spp.	35 (24.8)
<i>S. aureus</i>	27 (19.2)
CoNS.....	15 (10.6)
General surgery	
All BSI.....	137 (5.3) ^b
Monomicrobial BSIs	
<i>Klebsiella</i> spp.	29 (21.2)
<i>S. aureus</i>	24 (17.5)
<i>Acinetobacter</i> spp.....	19 (13.9)
Pediatric	
All BSIs.....	71 (2.8) ^b
Monomicrobial BSIs	
<i>S. aureus</i>	13 (18.3)
<i>Acinetobacter</i> spp.....	11 (15.5)
<i>Klebsiella</i> spp.	10 (14.1)
Neurosurgery	
All BSIs.....	71 (2.8) ^b
Monomicrobial BSIs	
<i>Acinetobacter</i> spp.....	10 (14.1)
<i>P. aeruginosa</i>	10 (14.1)
CoNS.....	10 (14.1)
Pediatric hematology/oncology	
All BSIs.....	60 (2.3) ^b
Monomicrobial BSIs	
CoNS.....	19 (31.7)
<i>Klebsiella</i> spp.	9 (15.0)
<i>Acinetobacter</i> spp.....	7 (11.7)
Cardiothoracic surgery	
All BSIs.....	39 (1.5) ^b
Monomicrobial BSIs	
<i>Klebsiella</i> spp.	7 (18.0)
<i>S. aureus</i>	6 (15.4)
<i>Acinetobacter</i> spp.....	5 (12.8)

^a The three pathogens most commonly isolated in each service.^b Percentage of the total of 2,563 BSIs at all study hospitals.

frequently isolated pathogens for all services, except neurosurgery, where *Acinetobacter* spp., *P. aeruginosa*, and CoNS were more frequently isolated.

In patients with monomicrobial BSI, the crude mortality ranged from 31.0 and 32.0 for *S. aureus* and CoNS, respectively (Table 2), to 52.1% and 68.8% for *Acinetobacter* spp. and *Candida* spp., respectively. In ICU patients, the crude mortality ranged from 46.5% and 48.2% for CoNS and *S. aureus*, respectively (Table 2), to 65.5% and 85.9% for *Acinetobacter* spp. and *Candida* spp., respectively. In patients with polymicrobial BSI, the crude mortality was 45.7%.

The mean time from hospital admission to onset of BSI due to the major pathogens ranged from 21 days and 22 days for *Acinetobacter* spp. and *S. aureus*, respectively, to 32 days for *Pseudomonas* spp. and enterococci.

Primary BSI, in which no source could be determined, was seen in 1,143 patients (44.6%). Secondary BSI originated from the lower respiratory tract in 362 patients (14.1%) and from the urinary tract in 186 patients (7.3%).

Of the 137 *Candida* isolates causing monomicrobial nBSI, nonalbicans species were more common than *Candida albicans*, accounting for 65.7%. The rank order of the major *Candida* spp. isolated was *C. albicans* (34.3%), *Candida parapsilosis* (24.1%), *Candida tropicalis* (15.3%), *Candida* spp. (10.9%), *Candida glabrata* (10.2%), *Candida krusei* (1.5%), *Candida pelliculosa* (1.5%), *Candida lusitanae* (0.7%), *Candida famata* (0.7%), and *Candida guilliermondii* (0.7%). Crude mortality was lowest for *C. parapsilosis* infection (51.5%) and highest for *C. krusei*, *C. pelliculosa*, and *C. lusitanae* (100%).

Antimicrobial susceptibility. Methicillin resistance was detected in 359 *S. aureus* isolates (43.7% of the tested isolates) and in 317 CoNS (86.4%). The proportion of *S. aureus* isolates with methicillin resistance was not significantly higher among ICU patients than among ward patients (49.3% versus 39.9%; *P* = 0.08). The first 62 samples of MRSA were confirmed by PCR for the *mecA* gene, and the SCCmec characterization revealed that 46.7% belonged to SCCmec type III, 24.1% to SCCmec type II, and 16.1% to SCCmec type IV. The SCCmec type III isolates were grouped as belonging to the Brazilian epidemic clone by PFGE. Three isolates carrying SCCmec type II showed 100% similarity to the New York-Japan clone.

Vancomycin resistance was found in 25% of 104 enterococ-

TABLE 4. Rates of antimicrobial resistance among Gram-positive organisms most frequently isolated from patients with nosocomial bloodstream infections

Antimicrobial drug	<i>S. aureus</i>		CoNS		<i>Enterococcus</i> spp.	
	No. of isolates	% Resistant	No. of isolates	% Resistant	No. of isolates	% Resistant
Ampicillin	ND ^a		ND		106	21.7
Methicillin	359	43.7	317	86.4	ND	
Cefazolin	163	34.4	162	85.2	ND	
Vancomycin	360	0	329	0.3	104	25.0
Teicoplanin	72	0	124	1.6	31	32.3
Linezolid	148	0	227	0.4	81	1.2
Ciprofloxacin	262	38.2	255	69.0	36	47.2
Clindamycin	359	47.4	323	75.9	ND	
Gentamicin	322	31.7	286	59.8	88	43.2

^a ND, not done.

cal isolates overall (Table 4), with 55.6% of *Enterococcus faecium* isolates and 17.6% of *Enterococcus faecalis* isolates resistant. The *vanA* gene was detected in 11 and 17 samples of *E. faecalis* and *E. faecium*, respectively. The *vanB* gene was not detected in these vancomycin-resistant isolates.

Antimicrobial resistance levels for the most common Gram-negative organisms causing nosocomial BSIs are shown in Table 5. Relatively high proportions of *Klebsiella* spp. displayed resistance to ampicillin-sulbactam, piperacillin-tazobactam, ceftazidime, and cefepime (54.5%, 33.5%, 54.4%, and 50.2%, respectively). Resistance to imipenem and meropenem was seen in 0.3% and 1.3% of the isolates. The molecular analysis of 94 extended-spectrum β -lactamase (ESBL)-positive isolates revealed the presence of *bla*_{TEM}, *bla*_{CTX}, and *bla*_{SHV} genes in 84 (89.3%), 86 (91.4%), and 68 (72.3%) strains, respectively. Among the carbapenem-resistant isolates, we detected the *bla*_{KPC} gene in 3 isolates.

For *Acinetobacter* spp., cephalosporins, aminoglycosides, fluoroquinolones, and carbapenems were not active against >50% of the isolates tested. We performed molecular analysis in 112 isolates resistant to carbapenems, and we detected the *bla*_{OXA23} gene in 85 isolates (75.9%).

Of the *P. aeruginosa* isolates, 33.9%, 36.6%, 42.9%, 36.8%, and 35.8% were resistant to piperacillin-tazobactam, ceftazidime, cefepime, imipenem, and meropenem, respectively. We detected the *bla*_{IMP} gene in 6 (10%) isolates and the *bla*_{SPM} gene in 24 (41%) isolates out of 59 carbapenem-resistant *P. aeruginosa* isolates.

DISCUSSION

Nationwide surveillance studies focusing on nosocomial infections are important tools that can discover specific issues related to antimicrobial resistance. Similar studies have been conducted in the United States and Europe, and relevant conclusions could be drawn from the data obtained (27, 29). The strength of such studies depends on the high correlation between etiologic agents and infection causation. As a result, bloodstream infection surveillance studies are preferable. Rigid and standardized clinical diagnostic criteria make data reliable and realistic, avoiding confounding colonizing agents not directly related to clinical disease.

Brazil is a country with more than 150 million inhabitants

TABLE 5. Rates of antimicrobial resistance among Gram-negative organisms most frequently isolated from patients with nosocomial bloodstream infections

Antimicrobial drug ^a	<i>K. pneumoniae</i>		<i>A. baumannii</i>		<i>P. aeruginosa</i>	
	No. of isolates	% Resistant	No. of isolates	% Resistant	No. of isolates	% Resistant
Amp-Sul	178	54.5	265	34.7	ND	
Pip-Tazo	281	33.5	148	75.7	174	33.9
Cefazolin	261	53.3	ND ^b		ND	
Ceftriaxone	202	55.4	ND		ND	
Ceftazidime	237	54.4	293	70.0	205	36.6
Cefepime	307	50.2	291	77.7	205	42.9
Imipenem	297	0.3	290	55.9	212	36.8
Meropenem	225	1.3	289	56.4	201	35.8
Ciprofloxacin	282	36.2	278	73.4	193	45.6
Gentamicin	290	30.7	272	51.8	184	45.7

^a Amp-Sul, ampicillin-sulbactam; Pip-Tazo, piperacillin-tazobactam.^b ND, not done.

and a total surface area larger than 8,500,000 km². In addition to its large area, the country has heterogeneous sociodemographic indicators, with wealthier regions concentrated in the southern part of the country. Although the majority of the population depends on the public health care system, an increasing fraction is being managed by private facilities. Heterogeneity is also reflected in health care practices at the level of nosocomial-infection management. As a result, different patterns of antimicrobial resistance and antimicrobial use may emerge within the country. Also, due to its intrinsic characteristics, etiologic agents and their respective antimicrobial susceptibilities may differ from the data in other countries.

A knowledge of the Brazilian data is of paramount importance for determining regional and national prevention and treatment strategies for nosocomial infections. Unlike previous nationwide network surveillance studies, the Brazilian SCOPE Study, similar to the U.S. SCOPE Study (29), is representative of the whole country, including data from its 5 different geographical regions. Also, standardized criteria for BSI were applied, conferring reliability for comparison with other studies.

Comparing Brazilian with American data, we found similar cohorts of patients, with very similar proportions of infection attributed to a central line, similar proportions of BSI originating in the ICU, and similar mean age and gender distributions. One striking difference was the observed bacterial etiology, with a much higher prevalence of Gram-negative versus Gram-positive bacteria (59% versus 34%). This finding was also seen in the EPIC II study (27), where the prevalence of Gram-negative pathogens in ICUs was 70% in South America compared to 49% in North America, considering all bacterial isolates from different body sites. As a tropical country, Brazil has higher average temperatures than the United States. In the 1970s and 1980s, some studies related higher temperatures (17, 24) to peak occurrences of infections, mainly due to *P. aeruginosa*. Recently, Perencevich et al. (22) in Maryland have reported higher rates of isolation of nosocomial Gram-negative bacteria (both fermentative and nonfermentative bacteria) in spring/summer than in fall/winter and an inverse relation for Gram-positive agents. Some previous studies point to the enhanced contact with water during warm weather to account for

this increase, but the theories are speculative rather than scientifically proven. Another possible explanation is the higher frequency of BSI episodes secondary to pulmonary and urinary sources than in the American study. On the other hand, irrespective of the cause, the prevalence of Gram-negative bacteria in Brazil has practical importance, especially when dealing with the issue of empirical treatment of suspected BSI, where, according to the present data, an agent directed at Gram-negative coverage is mandatory.

An even more striking difference is the very high percentage of infection due to *P. aeruginosa* and *Acinetobacter* spp. in the Brazilian cohort (21% versus 6%). However, it is important to mention that the U.S. SCOPE study occurred almost 10 years ago, and there have been increases in *Acinetobacter* infections in U.S. hospitals in recent years (11, 26). One other possible explanation is that the higher baseline prevalence of Gram-negative bacteria is related to enhanced use of anti-Gram-negative antibiotics, selecting for bacteria prone to develop multidrug resistance, such as nonfermentative Gram-negative bacteria. Also, the predilection for the respiratory tract of isolates of *P. aeruginosa* and *Acinetobacter* is another possible explanation. Again, the high prevalence of these agents may have a serious impact on antibiotic management, creating a vicious cycle of heavy use and resistance development.

Another important difference is the higher prevalence of nonalbicans *Candida* spp. in the Brazilian cohort. Although greater use of fluconazole is a possible explanation, the Brazilian cohort had a higher percentage of infections due to *C. parapsilosis* (24% versus 11% of all *Candida* infections). This could reflect less than optimal care for central lines in the Brazilian cohort, since the association of *C. parapsilosis* with catheter-related bloodstream infection is well documented (4, 9).

Antibiotic resistance within the group of Gram-negative bacteria is worrisome, especially regarding *P. aeruginosa* and *A. baumannii*. Rates as high as 56% resistance to carbapenems for *Acinetobacter* and 35% for *P. aeruginosa* are among the highest in the world's literature and have several implications for clinical practice (2, 15). Since resistance to carbapenems is usually associated with multidrug resistance (5), very few options remain viable. In some instances, polymyxins are the last alternative (21), and these drugs, already widely used in Brazil (16), could be considered in empirical therapy for the subgroup of patients prone to develop BSI due to these agents. *Klebsiella* spp. were the main enterobacteria isolated in our study, with a high level of ESBL-positive strains. KPC carbapenemase carriers were recently detected in Brazil (20).

S. aureus is the main cause of the bloodstream infections in the study, with a high level of methicillin resistance. Our molecular data reveal that SCCmec type III, belonging to the Brazilian epidemic clone, is still the most prevalent in our nBSIs; however, we show the introduction of SCCmec type II, and particularly of SCCmec type IV, *S. aureus* isolates in the hospital setting.

Very high crude mortality rates related to BSI were observed compared to the U.S. SCOPE Study (29). Antimicrobial appropriateness in BSI is a major factor related to survival (21) and could not be evaluated in the present study. This may play a role, since the rates of mortality caused by pathogens are considerably different in the two studies. On the other hand,

the study population composition may have an impact on the overall results. For instance, more patients with malignancy (24% versus 17%) and a higher proportion of multidrug-resistant organisms are present in the Brazilian cohort.

In conclusion, our study discloses a pattern of BSI in Brazilian hospitals that is considerably different from the American experience. A very high proportion of aerobic Gram-negative bacteria, very high rates of resistance to carbapenems by nonfermentative Gram-negative bacteria, higher mortality rates, and a shift to nonalbicans species of *Candida* were noted, and such findings may help Brazilian hospitals to develop their own guidelines for the treatment of BSIs.

ACKNOWLEDGMENTS

The study was funded in part by an independent medical grant provided by Pfizer, Inc. We also thank the Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP), Brasil (grant 2006/57700-0).

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